REMARKS

Claims 1-6 are pending. Claim 7 is cancelled without prejudice to the prosecution of its subject matter in other applications. Claims 8-21 which were withdrawn from consideration as being directed toward a non-elected invention are cancelled without prejudice to the prosecution of their subject matter in other patent applications. Claims 1 and 5 are currently amended. Since support for the amendments can be found throughout the specification and claims as originally filed, there is no new matter added as a consequence of the amendments to the claims.

Claim 7 is rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking enablement. Claims 1-7 are rejected under 35 U.S.C. § 112, second paragraph for being allegedly indefinite. Claims 1-7 are rejected under 35 U.S.C. § 103(a), as being allegedly unpatentable over Hoch *et al.* (U.S. Patent No. 6,043,045) in view of Dasgupta *et al.* (Tubercle and Lung Disease (2000): 80(3) 141-159). For reasons set forth below, it is respectfully requested that the rejections be withdrawn and that the claims be deemed allowable.

The Rejection under 35 U.S.C. § 112, ¶1 Should Be Withdrawn

Claim 7 is rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not reasonably provide enablement for identification of compounds that may be used to treat disease conditions caused by bacteria such as pneumonia, pertusis, listeriosis, enterobacterial diseases, and cholera. Claim 7 is cancelled without prejudice to the prosecution of its subject matter in other patent

applications. The basis for rejection of Claim 7 under 35 U.S.C. § 112, first paragraph is obviated and the rejection should therefore be withdrawn.

The Claims Are Definite

Claims 1-7 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. In particular, the phrase "such as" in Claim 7 allegedly renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. Claim 1 which reads on a two-component system of the of DevR-DevS and/or DevR-Rv2027c is allegedly indefinite since the degree of similarity encompassed in the term "homologues" is not clear and fails to delineate the scope of the two-component system. Thus Claims 2-7 dependent on Claim 1 are also rejected under 35 U.S.C. § 112, second paragraph. In addition, Claim 5 is rejected because the overexpression of proteins in *E. coli* in Claim 5 allegedly does not follow logically from Claim 1.

As a preliminary matter, Claim 7 is cancelled without prejudice; the basis for its rejection is therefore obviated and should be withdrawn.

Claim 1 is currently amended to read:

> "A method of SDS-PAGE based high throughput assaying for identifying drugs against mycobacterial species having two-component system of DevR-DevS and/or DevR-Rv2027c, said method comprising steps of:....."

Applicants respectfully suggest that Claim 1 as amended (i) does not contain the allegedly indefinite term "homologues"; and (ii) clearly defines the claimed subject matter of the two-component DevR-DevS and/or DevR-Rv2027c system. Claim 1 as

amended particularly points out and distinctly claims the claimed subject matter. The rejection of Claim 1 and dependent Claims 2-6 should therefore be removed.

The first step of a SDS-PAGE based high throughput assaying system for identifying drugs against mycobacterial species as set forth in Claim 1(a) is

"over-expressing DevR, DevS and Rv2027c and their single domain derivatives,".

This over-expression is in an *E. coli* system as set forth in dependent Claim 5. Because Claim 5 finds proper antecedence in Claim 1,it is not indefinite and the rejection should be withdrawn.

For the reasons set forth above, Applicants respectfully suggest that Claims 1-6 are fully enabled so the rejections under 35 U.S.C. § 112, second paragraph, should be withdrawn.

The Claims Are Not Obvious

Claims 1-7 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Hoch *et al.* (U.S. Patent Serial No. 6,043, 045; referred to henceforth as the '045 Patent) in view of Dasgupta *et al.* (Tubercle and Lung Disease (2000), 80(3):141-159). The Examiner alleges that (1) the '045 Patent discloses a high-throughput screen for identifying new antibiotic, antibacterial, or antimicrobial agents by inhibition of bacterial two-component systems using histidine protein kinase; and (2) Dasgupta *et al.* discloses the DevR-DevS two component system in Mycobacteria and homology of Rv2027c to DevS. It is further alleged that one of skill in the art would be motivated to apply the assay of the '045 Patent to the DevR-DevS two component system due to the shared phosphorylation reactions disclosed in both references and that

Dasgupta *et al.* concludes that the system would be a "novel target for anti-tubercular therapy."

The Applicants respectfully traverse the rejection. Preliminarily, the Examiner at page 7, paragraph 3 of the instant Office Action, has acknowledged that the '045 patent does not expressly disclose use of the method described therein for inhibition of the DevR-DevS or DevR-Rv2027c two component system in Mycobacteria nor the identification of anti-tuberculosis and anti-mycobacterial compounds.

Further, the '045 Patent effectively teaches away from the assay method of the instant invention. In the instant invention, Phosphorylated DevR (substrate) has a very short half-life and is rapidly dephosphorylated in the presence of DevS (sensor). This property is exploited to monitor phosphotransfer to DevR from DevS and the decay of the radiolabel therefrom without separating DevR from DevS. In the '045 Patent, SpoOF (substrate) is separated from the KinA (sensor) molecule and solid support-immobilized SpoOF is used to monitor presence of a reaction product. Thus the assay systems of the two inventions are based on distinct principles and compositions.

While the '045 Patent teaches a two-component assay system, there are significant variations among individual two-component kinase systems in terms of the kinetics of phosphorylation, half-lives of the phosphorylated form of the proteins and the mechanism of dephosphorylation of the response regulator components. These factors are critical in determining whether a particular system might be amenable to a specific utility including but not limited to the invention described in the '045 Patent or the instant

invention. Accordingly, a person of ordinary skill in the art would be aware of these critical variables and would not have been motivated to combine the assay of the '045 Patent to the DevR-DevS two component system merely due to the shared phosphorylation reactions disclosed in Dasgupta *et al.,* in seeking to meet the claimed invention. In addition, the proposed combination provides no reasonable expectation of success by reason of the critical variability between systems set forth above.

For the reasons set forth above, Applicants respectfully suggest that Claims 1-6 are not obvious over the cited references and the rejections under 35 U.S.C. § 103(a) should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request withdrawal of the outstanding rejections and allowance of the pending claims.

Applicants believe that no additional fee is required in connection with the submission of this document. However, should any fee be required, or if any overpayment has been made, the Commissioner is hereby authorized to charge any fees, or credit any overpayments made, to Deposit Account 02-4377. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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